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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,517	08/01/2001	Michael F. Clarke	060173-0014 (UMIP-003)	6988

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John Prince
McDermott, Will & Emery
28 State Street
Boston, MA 02109-1775

EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/04/2002 7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/920,517	Applicant(s) CLARKE ET AL.	
	Examiner Q. Janice Li	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-185* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-185* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S. C. 121:

I. Claims 1-30, and 32-40 are drawn to an isolated solid tumor stem cell or enriched population thereof, and a method of making such. Classified in class 435, subclass 325, and 374.

II. Claim 31 is drawn an enriched population of non-tumorigenic solid tumor cells. Classified in class 435, subclass 325.

III. Claims 41, and 126-130 are drawn to an *in vitro* method for the proliferation of a tumor stem cell. Classified in class 435, subclass 377.

IV. Claims 42, 131-136 and 148-171 are drawn to an *in vivo* method for the proliferation of tumor stem cells in an immune-competent or immunocompromised host, and a tumor bank produced by the method. Classified in class 424, subclass 93.1, and class 435, subclass 325.

V. Claims 43, 44, 46, 54-58, and 98-106 are drawn to an *in vitro* method of determining the effect of a testing agent on a solid tumor stem cell by contacting the tumor stem cell and testing compound and determining the effect of the testing compound on the TSCs. Classified in class 424, subclass 373.

VI. Claims 45, and 112-116 are drawn to an *in vivo* method of determining the effect of a testing compound on a solid tumor stem cell by administering the tumor stem cell and testing compound to a host and determining the effect on

the TSCs, wherein the testing agent may be a non-tumorigenic tumor cell. Classified in class 424, subclass 93.1, for example.

VII. Claims 47-53 and 59-61 are drawn to a method for stimulating an immune response to a solid tumor stem cell comprising introducing a population of ex vivo treated TSCs into a host in need of. Classified in class 424, subclass 93.1.

VIII. Claims 54-58 and 117-125 are drawn to a method for determining the effect of a test compound on a solid tumor stem cell by detecting complex formation between the test compound and the TSCs, wherein the testing agent could be an antibody. Classified in class 435, subclass 7.

IX. Claims 62-74 are drawn to a population of purified polynucleotides derived from TSCs. Classified in class 536, and subclass 23.1.

X. Claims 75-84 are drawn to a purified population of polypeptides derived from the TSCs. Classified in class 530, subclass 350.

XI. Claim 85 is drawn to a kit comprising a microarray of components selected from the group consisting of polynucleotides, polypeptides, and test compounds.

XII. Claims 86-91 are drawn to a method for analyzing gene expression patterns of enriched TSCs. Classified in class 435, subclass 6.

XIII. Claims 92-97 are drawn to a method for analyzing protein expression patterns of enriched TSCs. Classified in class 435, subclass 7.

XIV. Claims 98, and 107-110 are drawn to a method for determining the effect of a test compound on a solid tumor stem cell by testing compound microarray. Classified in class 435, subclass 287.2.

XV. Claims 98 and 111 are drawn to a method for identifying the target of a drug compound. Classification is to be determined depending on the method of identification.

XVI. Claims 137-147 are drawn to a method of genetically modifying TSCs in vitro and in vivo. Classified in class 424, subclass 93.21, and class 514, subclass 44.

XVII. Claims 172-177 are drawn to a chimeric mammal comprising a mammal and tumor stem cells. Classified in class 800, and subclass 8.

XVIII. Claims 178-185 are drawn to a method for modeling a tumor treatment regime comprising testing the effects of treatment regimens *in vivo* on tumor cells, wherein the therapeutic agent is an antibody against a Notch protein. Classified in class 424, and subclass 130.1, for example.

2. The inventions are distinct, each from the other because of the following reasons.

Inventions II, IV, IX-XI, XVII, and I are independent and distinct inventions. Inventions are distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions are drawn to different products, i.e. different types of tumor cells, polynucleotides, polypeptides, and chimeric animals. The different products possess distinct structures, belong to different chemical entities, have different mode of operation, different biological function, and require distinct technical considerations. For example, groups I

and II are drawn to different type of tumor cells, which have different cellular marker and distinct tumorigenicity.

Inventions X, XI, and IX are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed (a microarray of different components, such as cells, polypeptides, and testing agents), does not require the particulars of the subcombination as claimed because other components of group XI could lend patentability to the combination. The subcombination has separate utility such as polynucleotides of group IX could be used as a genetic vaccine.

Inventions III-VIII, XII-XVI, XVIII, and I are independent and distinct inventions. Inventions are distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different methods are drawn to TSC enrichment, expansion, drug screening, gene or protein analysis, genetic modification, and treatment regimen modeling, etc. For example, the *in vitro* expansion of TSCs (III) or the determination of a testing compound effect on a solid tumor stem cell (V) does not require the use of various animals (IV or VI). Groups V, VI, VIII, XIV, and XV are drawn to different ways of determining a testing compound effect on a solid tumor stem cell, however, group VIII requires detection of a complex

formation, group XIV requires microarray testing, and group XV requires identifying a drug target, each of these requirements is not practiced by other recited methods. Each of groups VII and XVIII is drawn to a method of treatment; however, the immune response recited for group VI is not required for group XVIII. The different methods use different starting material, different reagents, different test criteria, have different method steps, different modes of operation, and require distinct technical considerations.

Inventions IV-VIII, XII-XVI, XVIII, and I could be related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, group I is drawn to isolated tumor stem cells, and groups IV-VIII, XII-XVI, XVIII are drawn to various method of using such, which by itself shows that the product of group I could be used in materially different processes of using the product, wherein these methods could be practiced in a materially different process, e.g. the method for stimulating an immune response (group VI) could be practiced using a polynucleotide or a polypeptide functionally associated with a tumor antigen.

It is noted many of the independent and distinct inventions are recited as dependent claims, such as method claims 41-43, 84, and 111. However, these methods are distinct in terms of the intended use, method steps, materials used, and mode of operation. Therefore, they may have been restricted from the parent claims even though presented as dependent claims.

It is also noted that some of the groups may encompass multiple distinct inventions. For example, claims of group VIII are drawn to methods of detecting complex formation between the testing compound and the TSC, however, the method for detecting a complex of antigen-antibody is distinct from that of a RNA-antisense. Group XV is drawn to a method for identifying the target of a testing compound, depending on the nature of the target, e.g. an antigen, a receptor, a DNA binding protein, a transcription factor, etc., the method could be patentably distinct. Thus, upon election and further clarification, these groups may be subject to further restriction. They would be distinct inventions, not species election.

The differences of the Inventions I-XVIII are further underscored by their divergent classification and independent search criteria.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and different search criteria, it would impose an undue burden to the Office if all the groups are examined together, thus, restriction for examination purposes as indicated is proper.

3. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is advised that where a single claim encompasses more than one invention as defined above, upon election of an invention for examination, said claim will only be examined to the extent that it reads upon the elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
October 31, 2002

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER